

# Optimizing hepatitis B prevention and control

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## Societal relevance

In 2016 the World Health Organization (WHO) published the report 'Viral hepatitis 2016-2021 – towards ending of viral hepatitis' comparing viral hepatitis with other major communicable disease problems such as HIV, Malaria and Tuberculosis. To reduce the burden of disease of viral hepatitis WHO defined a set of priority actions. Targets for HBV were set at 95% reduction of new cases and 65% reduction in mortality by 2030<sup>4</sup> and WHO urged all countries to develop a national strategy to stop further transmission reduce the mortality and morbidity related to viral hepatitis. Based on the report the National Institute for Public Health and the Environment developed a National plan which scope it is to enhance initiatives regarding hepatitis control according to several themes (among others reduction of transmission through awareness and vaccination and identification). Chapters 2-5 matches the objective of the national plan on reduction of transmission through vaccination. The results of these chapters could be of interest for organizations involved in vaccination of adult risk groups for hepatitis B such as physicians working in infectious disease control, occupational physicians, addiction care professionals. As, in an adult population, depending on age and sex, 5% to 30% will not mount a protective immune response after vaccination, healthcare professionals will regularly encounter a non-responder after hepatitis B vaccination. We propose in this thesis an improved revaccination scheme for non-responders and offer a revaccination strategy based on a differentiated anti-HBs titre that results in a substantial reduction of vaccine use and vaccination consultations compared to the current revaccination policy. In addition chapter 2 describes some factors associated with better completion of a vaccination series in people who use drugs which can be used by addiction care facilities responsible for the vaccination of people who inject drugs.

All studies in this thesis were conducted in the light of this aim to reduce the burden of disease caused by the hepatitis B virus. The main thesis research questions originated on the one hand from day-to-day practice of infectious disease control from public health services in the Netherlands and on the other hand from ongoing prevention programs against hepatitis B in the Netherlands. These research questions are embedded in the infectious disease control which is a collaboration between regional (public health services and laboratories) and national (Centre for Infectious Disease Control as part of the National Institute for Public Health and the Environment) institutions. Consequently the findings from our studies have in addition to a scientific, also a value for infectious disease control guidelines of hepatitis B and the policy regarding primary and secondary prevention programs of hepatitis B.

For example, we used the information from chapter 4 to inform the National Platform of Infectious Disease Control (LOI) that is authorized to define guidelines of infectious disease control in the public health ('LCI-richtlijnen) in the Netherlands. We planned a revision of the paragraph regarding non-responders of the guideline

'Hepatitis B' based on the information from chapter 4 and 5 which was not completely available at the time of the first meeting.

The results and recommendations from chapter 7 were addressed to the Dutch Committee for Prevention of Iatrogenic Hepatitis B to reconsider their policy on exposure prone procedures for healthcare workers infected with hepatitis B.

### **Target groups**

In general the recommendations made on the hepatitis B (re)-vaccination policy and case finding of chronic hepatitis B patients is first of all of importance for public health professionals and policy makers. More specifically, public health professional, infectious disease specialists and policy makers involved on a national or regional level to reduce the mortality and morbidity related to viral hepatitis. The recommendations made regarding the vaccination policy are also of importance to all medical professionals that vaccinate risk groups against hepatitis B. For example, general practitioners, occupational practitioners and professionals in the field of addiction care or travel medicine.

### **Strengthen the public health services**

The results from chapter 3, 4 and 5 provide information to extent the knowledge base on hepatitis B vaccination in a more individualistic approach. The choice of vaccine and number of revaccinations depend on the individual characteristics and serological response. This individual revaccination approach fits in a development of regional health services to offer several vaccines, outside of national vaccination programs and travel consultations, to individuals with an indication for that vaccine ('Targeted vaccination' or in Dutch 'Vaccinaties op maat'). One of the novel research ideas is to further explore the influence of previous immunity of hepatitis A on the serological response of non-responders to hepatitis B vaccination. This will provide insights on a more targeted use of a combined hepatitis A and hepatitis B vaccine in the policy for non-responders after hepatitis B vaccination. Ultimately, the results of these studies will strengthen the available knowledge to use hepatitis B vaccines more tailored to the patient and enable the development of 'targeted vaccination' in public health services.

Since 2005, initially with funding from ZonMw, a collaboration between regional health services and academic centres 'Academische werkplaats Publieke Gezondheid' (AWP) started in the Netherlands. This collaboration reinforced contacts between these institutions to bridge the gap between the triangle of research, practice and policy in the field of public health. This collaboration provided an impetus to answer practice-based research questions of regional health services which is indispensable for the transformation of practice-based medicine into evidence-based medicine. The study described in chapter 4 was a collaboration of three AWP's and took an advantage of this growing network of public health services and academic centres. The study was also innovative as it modified the daily practice of a regional health

service by a few additional actions into a randomized trial. As it was a multicentre study, this enabled multiple regional health services to experience the conduct of a research question in practice. The study might as well demonstrate how to organise future infectious disease research in a practice-based setting.